Case No. 11320/33

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Miles B. Brennan *et al.*

Serial No: 10/764,712

Examiner: Angell, Jon E.

Filed: January 23, 2004

Group Art Unit: 1635

For: Method for Treatment of Insulin Resistance in Obesity and Diabetes

COMMISSIONER FOR PATENTS
ALEXANDRIA, VA 22313-1450

DECLARATION PURSUANT TO 37 CFR 1.132

I, Miles B. Brennan, declare as follows:

1. I received a Ph.D. in Biochemistry from Stanford University, School of Medicine in 1986.

2. I have been employed by the Eleanor Roosevelt Institute from July 1996 to June 2003 and by the University of Denver from July 2003 to the present. As an employee of Eleanor Roosevelt Institute and of the University of Denver, I have worked in the area of obesity research since 1996, and specifically worked on the development of a mouse model for studying and developing protocols for modifying the peripheral melanocortinergic pathways for controlling body weight and diabetes.

3. I am an inventor on the above-mentioned patent application.

4. I have read and understand the Office Action dated July 12, 2006 in the above-mentioned patent application.

5. I understand that the Examiner is of the opinion that based on the guidance presented in the specification, undue experimentation would be required to practice the claimed invention.

6. In order to demonstrate that the administration of an antagonist of MSH biological activity amerliorates the effects of insulin resistance and diabetes caused by insulin resistance, the following experiment was conducted under my direct supervision:

i. Ac-His-(pI) DPhe-Arg-Trp-NH_2 (JRH-322), a known MSH antagonist at the MCR 3 receptor, was reconstituted in DMSO to 1 mg/ml and stored frozen at -80 C in aliquots for injection. Prior to injection, an aliquot was thawed and diluted 1:10 in PBS for final concentration of 0.1 mg/ml PBS,

ii. at noon on days 1 to 10, three month old, female hyperglycemic obese (ob/ob) mice (3 mice per group) were each injected intraperitoneally (i.p.) with a total volume of 0.1ml of the JRH-322 preparation or with the same volume of with 0.1 ml PBS.

iii. wildtype or heterozygous littermates (+/?) were not so injected but were otherwise treated the same as the ob/ob mice,

iv. blood glucose levels were measured from a drop of blood from the tail vein of each mouse using Bayer Glucometer Elite test strips (Bayer, Elkhart, IN). Levels were measured under the following conditions:

a. Day 1. Mice were taken off food at 8AM, mice injected at 12 noon and the blood glucose measured about 1 hour later,

b. Day 9. Mice were injected at 12 noon and the blood glucose measured about 1 hour later, and

c. Day 10. Mice were taken off food at 8AM, mice injected at 12 noon and the blood glucose measured about 1 hour later,

v. In appendix 1, Figures 1, 2 and 3 should the glucose levels obtained in days 1, 9 and 10 respectively. On all three days, the glucose levels of the ob/ob mice treated with MSH antagonist were lower than those of the mice injected with PBS.

7. The above results demonstrate that treatment with the known MSH antagonist (JRH-322) causes a reduction in glucose levels in ob/ob mice as compared with control ob/ob mice,

8. The above results are fully reproducible,

9. The above experimental model is accepted by those skilled in the art as demonstrating the ability of a compound to amerliorate the effects of insulin resistance and diabetes caused by insulin resistance.

I declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above applications or any patent granted therein.

Miles B. Brennan

1 9 07

Date

Appendix 1

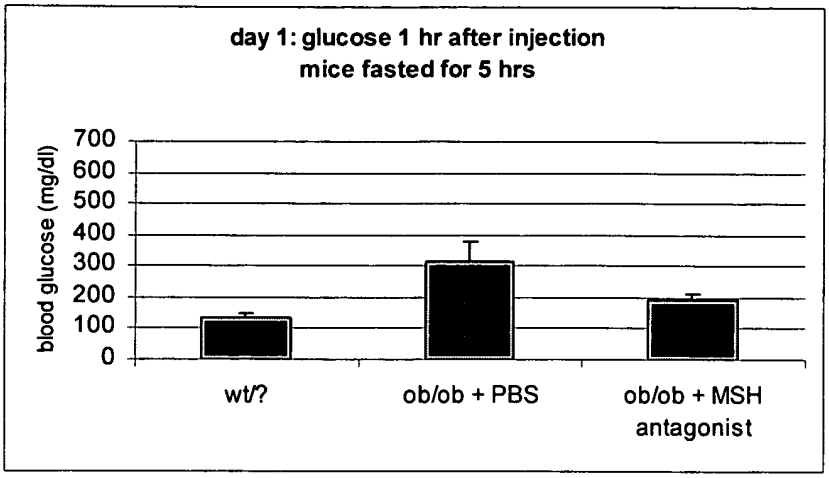

Figure 1

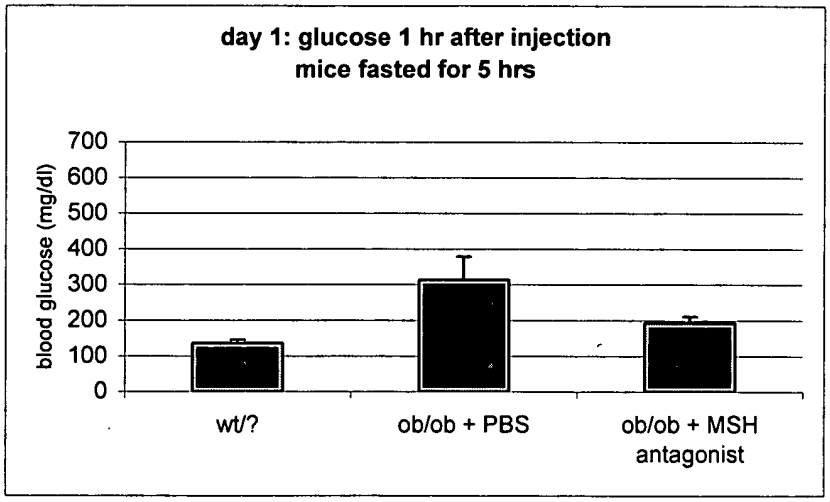

Figure 2

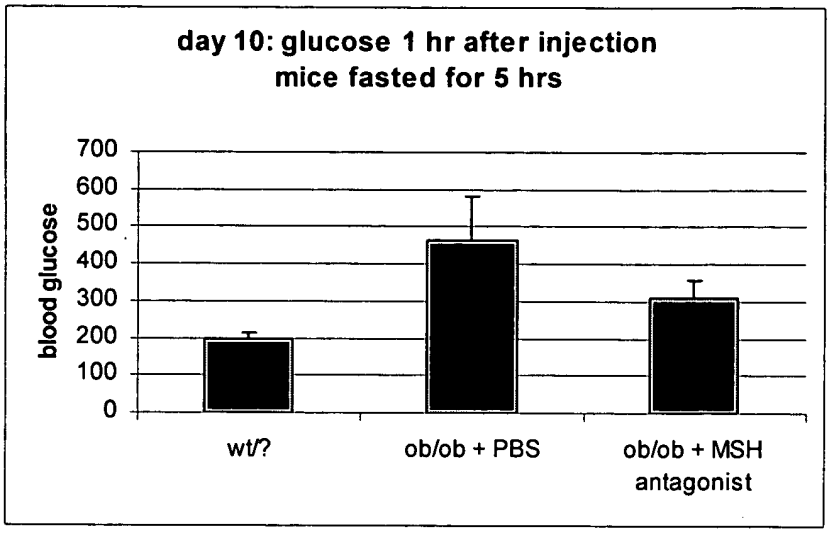
day 10: glucose 1 hr after injection
mice fasted for 5 hrs
blood glucose
700
600
500
400
300
200
100
0
wt/?
ob/ob + PBS
ob/ob + MSH
antagonist

Figure 3